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ALASKAN AIR COMMAND
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ABSTRACT

Glycine (amino-acetic acid) and other calorigenic, dietary adjuncts have received considerable attention recently and have been reported to modify whole body responses to cold exposure and hypothermia. In addition to any pharmacological action, the potential value of glycine and similar materials lies in their ability to provide additional calories to the cooling organism via the mechanism of specific dynamic action. Thirty grams of glycine were administered orally to five volunteer, male subjects who were subsequently exposed nude to an environment of 10° C. Measurements of rectal and extremity surface temperatures and whole body metabolic rates failed to show any statistically significant effects that could be attributed to the influence of glycine, as compared to glucose control measurements, throughout a 1-hour cold exposure. At this level of cold stress and drug dosage, glycine could not be seen to affect cold elicited, physiological responses and its values in mitigating human cold exposure is questioned. Reports of glycine effects for more severe cold stresses or during deep hypothermia may possibly be attributed to a more precipitous rate of heat loss, to a greater degree of cooling, or to other factors.

THE EFFECT OF GLYCINE ADMINISTRATION ON HUMAN RESPONSE TO AN ACUTE STANDARDIZED COLD STRESS*

In exposure to an acute or chronic cold stress, the thermoregulatory patterns and ultimate thermal state will depend largely on the avenues and gradients of heat exchange with the environment and the thermal resources of the individual. In addition to the organism's reduction of heat loss to the cold environment by appropriate physiological adjustments, the utilization of intrinsic thermogenic mechanisms will eventually determine the degree of success with which the stress is countered.

Increased muscular activity by voluntary exercise or by shivering, with a consequent elevation of oxygen consumption and whole body metabolic heat production, is one of the more readily employed mechanisms by which body heat stores can be replenished in a cold stress. With chronic cold exposure and subsequent cold acclimatization, the development of "chemical" thermogenesis further augments these stores in the acclimatized individual (Heroux, et al., 1956). The role of parallel stress states in this regard has received some attention (Adams and Heberling, 1958).

Attempts to elevate central body heat stores by the administration of glycine (amino-acetic acid) and other amino acids have resulted in considerable controversy over the effect of these agents on responses to a cold stress. It has been suggested that glycine operates through either calorigenic (Beavers and Covino, 1956; Best and Taylor, 1955) or vasomotor effects (Gubner, et al., 1947).

This study was designed to examine the effects of glycine on a human response to cold, and to evaluate the possibilities of its administration to cold-exposed personnel as an adjunct to any physiological defense mechanisms.

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METHODS

Five adult male, Caucasian volunteers from the tenant army units at Ladd AFB, Alaska were used as subjects. These individuals remained on detached duty with the laboratory for several months during which time they participated in other experimental programs (Adams and Heberling, 1958; Minium and Owens). By the time this study was initiated, the subjects were well aware of the standard methods of data recording, equipment, and procedures. For this reason it is believed that emotional stress and anxiety were negligible.

The physiological responses of the subject group in an acute cold stress were examined with and without glycine feeding. By using the same personnel in each group at different times, the glycine responses could be compared to glucose measures in the same individuals. Morning and afternoon cold-room exposures were alternated for each individual in order to minimize the effect of diurnal variations in the responses.

Each subject reported to the laboratory in a resting and postabsorptive state. The experimental dosage consisted of 30 grams of powdered glycine dissolved in water and flavored with lemon concentrate; the control mixture of an equal volume of water and flavoring was sweetened with sugar (glucose). The glycine (or glucose) potion was ingested leisurely and without forcing during a 20- to 30-minute period.

Each subject rested at a comfortable room temperature (70° F) while drinking the prepared liquid. This time, plus the half hour devoted to experimental preparation, allowed adequate time for the subject to assimilate the test material and to become thermally adjusted to a neutral ambient temperature.

The nude subject was prepared with the recording equipment outside the cold room and covered with two woolen blankets. After a stable thermal level was reached (as indicated by rectal and skin temperature measurements) the test subject was carried into the cold chamber on a nylon wire mesh litter, but remained covered with the blankets until 10-minute control measurements were established. The blankets were then removed and the hour-long exposure began.

The cold chamber was maintained at a temperature of $10^{\circ} \pm 0.5^{\circ}$ C. Air movement in the chamber during the cold-exposure period for each subject

was adequate to maintain air circulation, but small enough to be considered physiologically negligible.

Trunk and extremity surface temperatures were recorded with 22 copper-constantan (30 gauge) thermocouples. Body temperatures were recorded continuously throughout the control and exposure periods by automatic, strip chart potentiometers. Average skin temperatures were calculated from an equation based on the original Hardy and DuBois method (1938). The slightly modified estimate consisted of a greater number of temperature samples by the use of additional thermocouples.

Internal body temperatures were recorded with a Yellow Springs thermistor rectal probe inserted 10.0 cm into the rectum. Average body temperatures were estimated using the following guide:

$$ABT = 0.6\ T_r + 0.4\ T_s$$

where:

ABT = average body temperature

T_r = rectal temperature

T_s = average skin temperature

The open circuit, indirect calorimetric technique consisted of a Gasuhr respirometer, Beckman Oxygen analyzer and associated recording equipment. These sampling and recording procedures are described in greater detail elsewhere (Adams and Rennie, 1957). Total body heat production, expressed as cal/hr/M^2, was estimated with the calculation outlined by Wier (1949).

RESULTS AND DISCUSSION

The physical measurements for each subject used in this design are presented in Table I.

These data are presented in lieu of skin-fold measurements or other more specific assessments and indicate homogeneity with regard to age, height, weight, and surface area of the subjects used in this study.

TABLE I

PHYSICAL MEASUREMENTS OF
EXPERIMENTAL SUBJECTS

Subject	Age (yrs)	Height (ins)	Weight (lb)*	S A (M^2)**
A	19	67	157	1.82
B	22	69	157	1.86
C	19	68	150	1.86
D	19	68	141	1.76
E	24	69	152	1.82
Average	20	68	151	1.82

*Average weight throughout program.

**Determined by nomograph (Wier, 1949).

Each of the 6 criteria (hand, foot, toe, average skin, rectal temperature, and metabolic rate) involved 30 measurements obtained from 5 subjects under 6 combinations of 2 drugs, and 3 exposure comparisons. The statistical operations performed on each criterion, therefore, involved the computation of population variance estimates for each identifiable component of the total variation, F tests of significance of the main effects and their interactions, and, where indicated, t tests of the significance of simple effects.

The analysis presented in Table II indicates no significant drug (glycine) effect for any subject on the criteria studied.

TABLE II

ANALYSIS OF VARIANCE OF CRITERION MEASUREMENTS

Source df		Subjects 4	Drugs 1	Times 2	DT 2	SD 4	ST 8	SDT 8
Toe Temp °C	σ^2 F	12.3450	3.4000 <1.0	160.0750 825.98*	1.1200 1.75	9.9700 15.61*	0.1938 <1.0	0.6388
Foot Temp °C	σ^2 F	10.1225	2.5800 <1.0	150.4500 520.95*	0.0650 <1.0	4.7825 16.28*	0.2888 <1.0	0.2938
Hand Temp °C	σ^2 F	1.9750	0.5300 <1.0	84.8450 49.91*	1.3650 <1.0	4.4150 1.56	1.7000 <1.0	2.8300
Rectal Temp °C	σ^2 F	0.7800	0.1200 <1.0	0.0450 7.26*	0.0100 <1.0	0.1625 10.03*	0.0062 <1.0	0.0162
Avg Skin Temp °C	σ^2 F	0.6900	0.0100 <1.0	74.0250 1558.42*	0.0350 <1.0	0.2350 3.24	0.0475 <1.0	0.0725
Metabolic Rate Cal/hr/M^2	σ^2 F	79.6175	4.0300 <1.0	654.3000 49.04*	36.2350 2.10	55.9500 3.24	13.3413 <1.0	17.2625

*P < 0.05

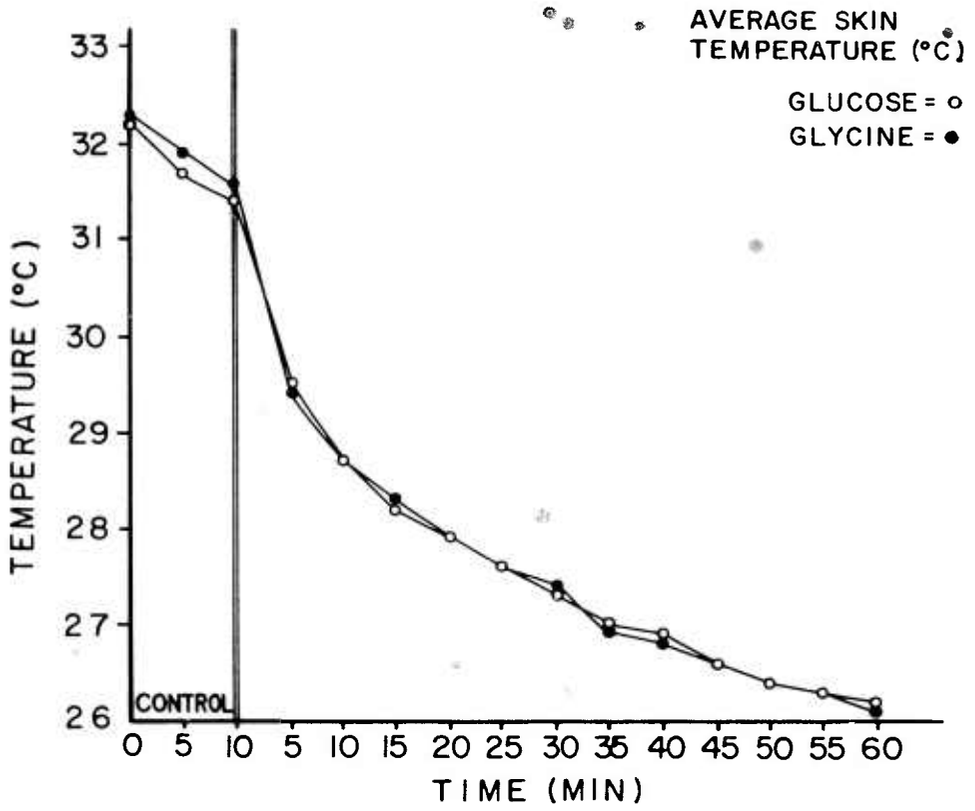

Figure 1. Average skin temperatures under glucose and glycine treatment.

Figure 1 presents graphically the average skin temperature measurements calculated from integrated surface temperatures as suggested by Hardy and DuBois (1938). Although this value decreases slightly during the control period of observations in the cold room, average skin temperatures for the five subjects are nearly identical throughout the remainder of the cold exposure and do not prove to be statistically significant ($P > 0.05$) at any time during the experiment.

The physical characteristics of any single respondent may well modify physiologic responses to a cold stress. Table I suggests that any inter-subject variability in cold-room responses is not attributable to large inter-group differences in these physical measurements. Since the same subjects were used in both the glucose and glycine portions of the test, any differences in cold-room response cannot be attributed to physical differences.

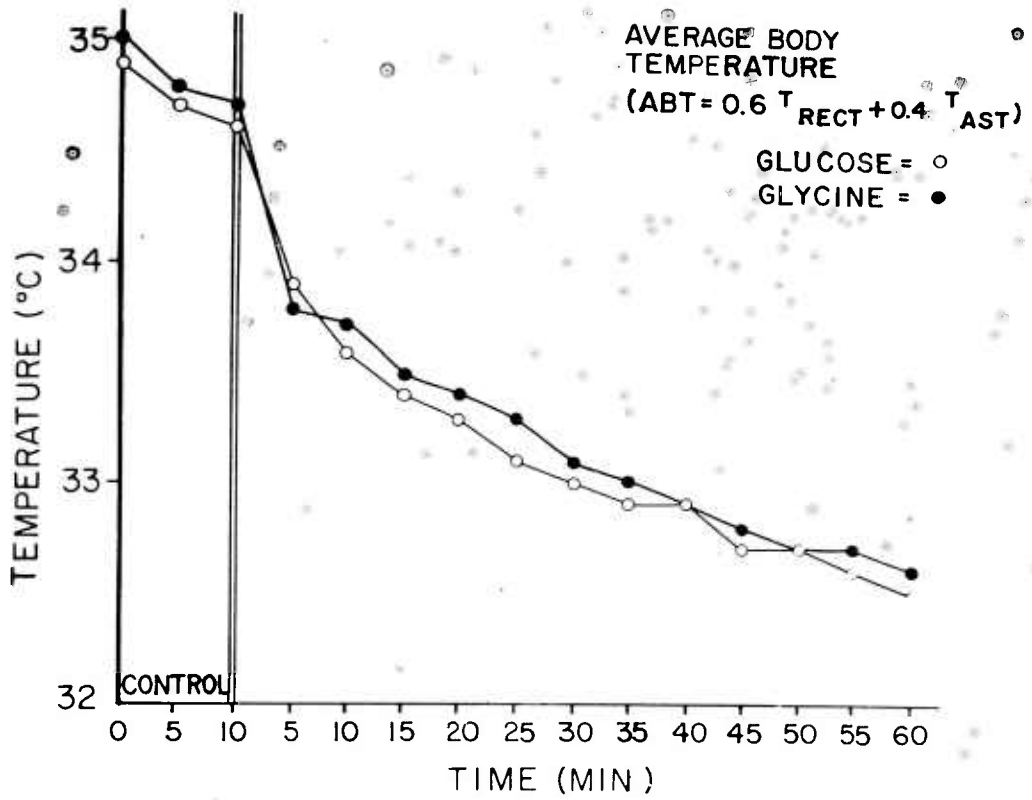

Figure 2. Average body temperature under glucose and glycine treatment.

Any pronounced effect of glycine should be seen in either an evaluation of total body heat content indexed by average body temperature (Fig. 2) or in an estimation of average skin temperature (Fig. 1). No statistically significant group differences are demonstrable at any point in either of these measures during the cold-exposure period. In fact, the measures of average skin and average body temperature appear to be remarkably similar (if not identical) within the limits of experimental error, during the cold exposure.

lt is possible that the calorigenic effect of glycine, via the poorly understood mechanism of "specific dynamic action" might be operating at the level of deep body rather than extremity temperature. Although the limitations of rectal temperature as a precise indicator of deeper body temperature are recognized (Meade and Bommarito, 1949), this measure might be expected to reflect central body temperature reasonably well at these levels of cooling.

It is readily admitted that a 0.5° C change in rectal temperature might be more important physiologically than a difference of the same magnitude in a more peripheral body area, for instance the hand (LeBlanc, 1956). The observation of a "slight benefit" reflected in rectal temperature with glycine feeding, in the absence of other consistent changes of cold response measurements, has been reported earlier (Carlson, et al., 1958). A casual inspection of rectal temperature differences seen in Table III would seem to indicate agreement with the above report. However, rectal temperature, as well as all other parameters shown in Table III, do not prove to be statistically different.

TABLE III

AVERAGED RESPONSES DURING COLD EXPOSURE*

	Time During Exposure					
	Control*		30 minutes*		60 minutes*	
Measure	Glucose	Glycine	Glucose	Glycine	Glucose	Glycine
Hand (°C)	27.2	26.0	21.9	21.6	20.3	19.4
Foot (°C)	28.7	29.3	22.4	23.2	20.1	20.6
Toe (°C)	22.7	24.0	16.6	16.8	14.6	14.8
Rectal (°C)	36.8	36.8	36.9	37.0	36.7	37.0
ABT (°C)	34.8	34.8	33.0	33.1	32.5	32.6
MR ($Cal/hr/M^2$)	38.0	42.0	53.0	49.0	60.0	59.0

*Differences reported in this table are not statistically significant at the 0.05 level (analysis of variance).

An effective glycine response in human cold exposures might be expected to be reflected in gross performance as well as in other physiological measures. Data are currently available to indicate that operational efficiency under a cold stress (as determined on the USAF SAM Multidimensional Pursuit Test) is not enhanced by glycine feeding (Payne). Earlier reports have also shown certain limitations to the use of glycine (Keys, 1943).

These data are not necessarily in conflict with published observations that glycine is effective in hypothermia (Beavers and Covino, 1956) considering the differences in experimental design, test animals, route and dosage of the test material, and degree of cooling.

The data presented in this report can be considered to represent a random distribution of measurements, in that there is no discernible correlation between the measures obtained and the treatments applied. From these data, then, there is no observable evidence for the alleged benefit of glycine on human response to a limited cold stress.

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